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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,383	06/26/2006	Kyu Hyun Lee	5804900032	3667

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,383	LEE ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23 are pending and currently under examination.

Specification

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-23 are rejected under 35 U.S.C. 101 because claim is drawn to non-statutory subject matter as follows:

Claims 1-23 are drawn to an anticancer agent encompassing any 'cells harboring human apolipoprotein (a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) gene'. Such a recitation in its breadth reads on the cells of a live human since all human cells naturally harbor said gene or a part of it. Further it is PTO policy not to allow claims to humans (1077 O.G. 24 April 1987). The insertion of a phrase such as 'an isolated host cell', or 'a cultured mammalian/or human cell' or 'cell of a non-human mammal' or 'excluding human organism' would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition or agents of human apolipoprotein (a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) and a method of treating sold tumors with AAV viral vectors as gene carriers and administered to site of solid tumors by direct injection, does not enable any other gene carrier, and any method of administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At issue, under the enablement requirement of 35 U.S.C. 112, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). These factors include, but are not limited to: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the prior art; (4) The level of one of ordinary skill; (5) The level of predictability in the art; (6) The amount of direction provided by the inventor; (7) The existence of working examples; and (8) The quantity of experimentation needed to make or use the invention based of the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). All of the wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below as to show that one of the ordinary skill in the art have to go through "undue experimentation" in order to practice the invention.

Nature of the invention: The invention relates to gene therapy compositions and methods using human apolipoprotein (a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) gene for treating cancer.

Breadth of the claims And Guidance Provided in the Specification: The scope of the invention encompasses a method of gene therapy of any cancer with recombinant human apolipoprotein (a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) gene using any kind of gene carrier (cells, viruses, naked DNA etc) and administered by any route of administration.

The specification only teaches the enabled use of a AAV-viral vector gene carrier for introducing recombinant human apolipoprotein (a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) and a method of administration of the same by direct injection of recombinant virus and treating a solid tumor.

The specification does not teach any enabled examples of other viral vectors or cells as carriers of the gene for treating any cancer and further does not teach enabled examples of any chemical method, physical method, or using liposome as a method of administration.

In the absence of representative number of enabled examples in the specification commensurate with the breadth of the claims one of ordinary skill in the art would conclude that the invention is unpredictable and would require undue experimentation to practice the invention in its full scope. Applicants' attention is drawn to In re Shokal, 242 F.2d 771, 113 USPQ 283 (CCPA 1957). The test is whether the number of claimed genus/or species of gene carriers and method of delivery and etc., as instantly claimed and prior to the reference date or the date of the activity provided an adequate basis for inferring that the invention has generic applicability.

The level of one of ordinary skill in the Art at the Time of Invention: The level of one of ordinary skill in the art at the time of filing of the instant application is high requiring an advanced degree or training in the relevant field. The status of the art at the time of filing was such that said skilled in the art would not have been able to make or use the invention for its fully claimed scope without undue experimentation.

***State of the Art, the Predictability of the Art*:** At about the effective filing date of the present application art is unpredictable with regard methods of gene transfers in vivo using both viral and non-viral vectors, as has been claimed in the instant invention, art is still unpredictable with regard to efficacy, specificity and safety. Gene therapy or in vivo gene transfers are still considered to be highly experimental area of research and it has been difficult to predict the out come of many therapeutic genes and vector systems because of various factors that govern the expression, therapeutic potential of the transduced genes, and the undesirable host immune reactions etc., in vivo (Reviewed in Goncalves et al, Bioessays, 2005, 27: 506-517). In addition there exists

an unpredictability about the degree to which a foreign gene or vector would interfere with cellular genetic material as observed in treatment of X-SCID patients " These serious adverse events presented as a leukemia-like syndrome were surprising since the risk of insertional oncogenesis was considered to be negligible based on previous trials and on the perceived, though not universally accepted, notion of random retroviral integration" (Goncalves, Bioessays, 2005, 27: 506-517, p. 514, col.2, 1st ¶). Thus the unpredictability in the art, at the time of instant filing, regarding the methods and consequences of claimed ex vivo and in vivo gene therapies of central nervous system is such that one of ordinary skill in the art finds the claimed invention highly unpredictable and cause undue experimentation to practice the invention in its full claimed scope.

Amount of experimentation necessary: Because of the lack of working examples, insufficient guidance and direction provided by Applicant, the inherent unpredictability of the art, and the nature of the invention, one of skill in the art would be required to perform a large amount of experimentation to make and/or use the invention in its full scope as claimed by Applicant. Such experimentation would be required to make sufficient number of gene carriers including various viral vectors, plasmid constructs and cells expressing appropriate Kringle peptides and deliver them in various modes in to a subject and assess their efficacy in delivering the gene to target tissue namely cancer cells. Further one of ordinary skill has to assess the in vivo effects, both short term and long term, of the different viral vectors or gene carrier cells on the subject health and immunity. Further these claims are not enabled because one of skilled in the art, at the date of filing, would not be able to rely upon the state of the art in order to successfully predict a priori the in vivo effects of claimed gene carriers and efficacy of various delivery routes. Accordingly, in view of the lack of teachings in the art and lack of guidance provided by the specification with regard to an enabled use of sufficient number of gene carriers and delivery methods as of around the filing date of instant application and for the specific reasons cited above, it would have required undue experimentation for one of skill in the art to make and use the full scope of the claimed invention. At the best the specification as filed is found only enabled enabling for compositions of gene

therapy and a method providing a Kringle polypeptide gene by directly injecting an AAV vector encoding human apolipoprotein (a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) gene for treating cancer.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1,3-4, 6 and 16 are rejected under 35 USC 102 (b) as being anticipated by Trieu et. al (1999, Biochem. Boiphys. Res. Comm. 257: 714-718).

The above claims are directed to an anticancer agent containing a gene carrier or cell harboring human apolipoprotein kringle KIV9-KIV10-KV (LK68) or KV (LK8) and in further limitations carrier is a vector or a recombinant virus and the cells harboring vector including hematopoietic stem cells, dendritic cells and to a method of for the prevention or the treatment of a solid tumor including its growth or metastaisis by administering said gene carrier

Regarding claims 1, 3-4, 6 and 16 Trieu teaches that there is an established link between cancer and Apo(a) (the protein that contains KIV9-KIV10-KV (LK68) or KV (LK8)) levels and reports that Lews lung carcinoma (LL/2) lcancer cells show a delayed growth of tumor and reduced angiogenesis when provided with apo(a) transgene. Trieu teaches provding CHO-K1 cells over expressing truncated human apo(a) transfected using a vector. Trieu further teaches full length recombinant apo(a) causes tumor suppression (p.714, abstract, col.2, 1st paragraph, 3rd paragraph; p.715, col.1 3rd paragraph, col.2, 1st paragraph; p.716, Fig.2). The cited art thus anticipates the invention as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 12-14 and 20 of Application No. 10/162,817 (USPTO Pub No.: US2006/0013823A1).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim because the examined claim is either anticipated by, or would have been obvious over, the reference claim.

The subject matter claimed in the instant application is covered by the cited application. The cited application teaches gene therapy using vectors and cells carrying expressible nucleic acids coding for KIV9-KIV10-KV (LK68) or KV (LK8) (p.7 paragraphs 0087 0089) and the delivery of said vectors and recombinant viruses and cells expressing the recombinant said gene to patient (p.8 paragraphs 0090-0096) for treating cancer (paragraph 0088 and claims 12 and 20). Although claimed as a component agent in gene therapy of cancer it is clear from the description in the

specification that gene therapy of a cancer (including tumor metastasis) can be carried out using a vector that expresses LK8 or LK68 as an effective ingredient in said cancer therapy. The claims in the cited application and the instant claims are therefore considered to be obvious of one another. Thus it would have been obvious to one of ordinary skill in the art that the cited claims in the instant invention and the cited application are one and the same.

Accordingly, the claimed process in the present application and the cited patent are obvious variants. Therefore, the inventions as claimed are co-extensive. This is provisional obviousness double patenting rejection since the cited claims have not yet been patented.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is ***571 272-0548.*** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you

are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

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